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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/737,476	12/18/2000	Leo G.J. Frenken	P 0275850 T 7060C	9341
9629	7590	12/29/2005	EXAMINER	
MORGAN LEWIS & BOCKIUS LLP 1111 PENNSYLVANIA AVENUE NW WASHINGTON, DC 20004			COLLINS, CYNTHIA E	
			ART UNIT	PAPER NUMBER

1638

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/737,476

Applicant(s)

FRENKEN ET AL.

Examiner

Cynthia Collins

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on September 28, 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-13 and 16 is/are pending in the application.
- 4a) Of the above claim(s) 8 and 10-13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7,9 and 16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

Applicant's submission filed on September 28, 2005 has been entered.

Claims 14-15 are cancelled.

Claim 1 is currently amended.

Claim 16 is newly added.

Claims 8 and 10-13 are withdrawn.

Claims 1-13 and 16 are pending.

Claims 1-7, 9 and 16 are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

### ***Claim Objections***

Claim 16 is objected to because of the following informalities: the word "chloroplast" is misspelled. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1, and claims 2-7, 9 and 16 dependent therein, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is

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indefinite in the recitation of “said cellular compartment” in line 8. There is insufficient antecedent basis for this limitation in claim 1.

***Claim Rejections - 35 USC § 102***

Claims 1, 2, 7 and 9 remain rejected, and claim 16 is rejected, under 35 U.S.C. 102(b) as being anticipated by Casterman et al. I (WO 94/04678, 3 March 1994, Applicant's IDS), for the reasons of record.

Applicants' arguments filed September 28, 2005 been fully considered but they are not persuasive.

Applicants traverse the rejection, and maintain that in order to expedite prosecution, they have amended claim 1 to recite producing functional heavy chain immunoglobulins in a plastid of a plant. Applicants maintain that because the cited reference does not disclose expression of heavy chain immunoglobulins in a plastid, the rejection should be withdrawn (reply page 5).

Applicants' argument is unconvincing. The amendment of the preamble of claim 1 to recite “producing in a plastid” does not overcome the rejection, as the preamble limitation is an intended use of the claimed method. Because the method set forth in the body of claim 1 imposes no requirement for the production or expression of heavy chain immunoglobulins in a plastid, the method of Casterman et al. I anticipates the claimed method.

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Claims 1, 2, 5, 7 and 9 remain rejected, and claim 16 is rejected, under 35 U.S.C. 102(b) as being anticipated by Casterman et al. II (US Patent No. 5,759,808, issued June 2, 1998), for the reasons of record.

Applicants' arguments filed September 28, 2005 been fully considered but they are not persuasive.

Applicants traverse the rejection, and maintain that in order to expedite prosecution, they have amended claim 1 to recite producing functional heavy chain immunoglobulins in a plastid of a plant. Applicants maintain that because the cited reference does not disclose expression of heavy chain immunoglobulins in a plastid, the rejection should be withdrawn (reply pages 5-6).

Applicants' argument is unconvincing. The amendment of the preamble of claim 1 to recite "producing in a plastid" does not overcome the rejection, as the preamble limitation is an intended use of the claimed method. Because the method set forth in the body of claim 1 imposes no requirement for the production or expression of heavy chain immunoglobulins in a plastid, the method of Casterman et al. II anticipates the claimed method.

### ***Claim Rejections - 35 USC § 103***

Claims 1, 3, 4, 7 and 9 remain rejected, and claim 16 is rejected, under 35 U.S.C. 103(a) as being unpatentable over any of Magnuson et al. (Protein Expression and Purification, 1996, Vol. 7, pages 220-228) or Casterman et al. I (WO 94/04678, 3 March 1994, Applicant's IDS) or Casterman et al. II (US Patent No. 5,759,808, issued June 2,

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1998), in view of Owen et al. (Biotechnology, Vol. 10, pages 790-794, July 1992), for the reasons of record.

Applicants' arguments filed September 28, 2005 been fully considered but they are not persuasive.

Applicants point out that they have amended claim 1 to recite producing functional heavy chain immunoglobulins in a plastid of a plant. In addition, Applicants point out that none of the cited references mention or even suggest producing immunoglobulins in the plastid of a plant, and further point out that Maruson et al., Casterman I and Casterman II teach that an endoplasmic reticulum targeting sequence is necessary to produce functional antibodies in plants. Applicants also point out that Hiatt et al. strongly indicates that expression in ER may be required for immunoglobulin assembly in plants. In addition, Applicants point out that Owen et. al. specifically indicates that ER signal sequences "appear to be required" in plants in order to produce functional antibodies". (reply pages 6-7)

Applicants' argument is unconvincing. The amendment of the preamble of claim 1 to recite "producing in a plastid" does not overcome the rejection, as the preamble limitation is an intended use of the claimed method. Because the method set forth in the body of claim 1 imposes no requirement for the production or expression of heavy chain immunoglobulins in a plastid, the cited references need not teach or suggest the production or expression of heavy chain immunoglobulins in a plastid in order to render the claimed method obvious. Further, the method set forth in the body of claim 1 does not exclude the targeting of heavy chain immunoglobulins to the endoplasmic reticulum.

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Claims 1, 3, 5, 7 and 9 remain rejected, and claim 16 is rejected, under 35 U.S.C. 103(a) as being unpatentable over any of Magnuson et al. (Protein Expression and Purification, 1996, Vol. 7, pages 220-228) or Casterman et al. I (WO 94/04678, 3 March 1994, Applicant's IDS) or Casterman et al. II (US Patent No. 5,759,808, issued June 2, 1998), in view of Le Gall et al. (Applied and Environmental Microbiology, Vol. 64, No. 11, pages 4566-4572, November 1998), for the reasons of record.

Applicants' arguments filed September 28, 2005 been fully considered but they are not persuasive.

Applicants point out that they have amended claim 1 to recite producing functional heavy chain immunoglobulins in a plastid of a plant. In addition, Applicants point out that none of the cited references mention or even suggest producing immunoglobulins in the plastid of a plant, and further point out that Maruson et al., Casterman I and Casterman II teach that an endoplasmic reticulum targeting sequence is necessary to produce functional antibodies in plants. Applicants also point out that Hiatt et al. strongly indicates that expression in ER may be required for immunoglobulin assembly in plants. In addition, Applicants point out that Le Gall specifically indicates that their vector construction included the leader sequence pelB which would express the scFv via the secretory pathway (i.e., via the ER), further supporting that an ER leader sequence is required.. (reply page 7)

Applicants' argument is unconvincing. The amendment of the preamble of claim 1 to recite "producing in a plastid" does not overcome the rejection, as the preamble limitation is an intended use of the claimed method. Because the method set forth in the body of claim 1 imposes no requirement for the production or expression of heavy chain

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immunoglobulins in a plastid, the cited references need not teach or suggest the production or expression of heavy chain immunoglobulins in a plastid in order to render the claimed method obvious. Further, the method set forth in the body of claim 1 does not exclude the targeting of heavy chain immunoglobulins to the endoplasmic reticulum.

Claims 1, 3, 6, 7 and 9 remain rejected, and claim 16 is rejected, under 35 U.S.C. 103(a) as being unpatentable over any of Magnuson et al. (Protein Expression and Purification, 1996, Vol. 7, pages 220-228) or Casterman et al. I (WO 94/04678, 3 March 1994, Applicant's IDS) or Casterman et al. II (US Patent No. 5,759,808, issued June 2, 1998), in view of Artsaenko et al. (The Plant Journal, Vol. 8, No. 5, pages 745-750, 1995), for the reasons of record.

Applicants' arguments filed September 28, 2005 been fully considered but they are not persuasive.

Applicants point out that they have amended claim 1 to recite producing functional heavy chain immunoglobulins in a plastid of a plant. In addition, Applicants point out that none of the cited references mention or even suggest producing immunoglobulins in the plastid of a plant, and further point out that Maruson et al., Casterman I and Casterman II teach that an endoplasmic reticulum targeting sequence is necessary to produce functional antibodies in plants. Applicants also point out that Hiatt et al. strongly indicates that expression in ER may be required for immunoglobulin assembly in plants. In addition, Applicants point out that Artsaenko states that they employed an ER targeting sequence as well as a KDEL retention sequence in order to express and retain the immunoglobulin in the ER, and further indicate that expression in



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the ER appears to be necessary to produce active antibody in an amount necessary to produce a measurable effect. (reply page 7)

Applicants further maintain that all the cited art teaches away from the present invention and a person of ordinary skill would not have been motivated to target expression of heavy chain antibodies as recited in the present application to plastids. In addition, as discussed on page 6 lines 6 to 14 of the specification as filed, Applicants point out that previous attempts to express other types of antibodies in chloroplasts have failed, and that the specification discloses that expression of scFv in plastids is unstable and has an adverse effect on plastid structure and function (Example 6 and Figure 8), whereas expression of functional VHH antibodies was successful (Examples 5 and 13 and Figure 4) with high levels of expression obtained (1.0% and 0.3% of soluble protein extracted - see page 47 lines 17 to 30 and page 56 lines 26 to 34).. Applicants maintain, therefore, that there would have been no reasonable expectation of success for a person of ordinary skill to generate the claimed invention. (reply pages 7-8)

Applicants' argument is unconvincing. The amendment of the preamble of claim 1 to recite "producing in a plastid" does not overcome the rejection, as the preamble limitation is an intended use of the claimed method. Because the method set forth in the body of claim 1 imposes no requirement for the production or expression of heavy chain immunoglobulins in a plastid, the cited references need not teach or suggest the production or expression of heavy chain immunoglobulins in a plastid in order to render the claimed method obvious. Further, the method set forth in the body of claim 1 does not exclude the targeting of heavy chain immunoglobulins to the endoplasmic reticulum.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-7, 9 and 16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 and 11-12 of copending Application No. 11/267,191, filed November 7, 2005. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending claims and the claims of copending Application No. 11/267,191 both encompass the introduction of immunoglobulin heavy chain coding sequences into plant cells and plants produced by such methods .

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

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Claims 1-7, 9 and 16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 and 11-12 of copending Application No. 11/267,310, filed November 7, 2005. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending claims and the claims of copending Application No. 11/267,310 both encompass the introduction of immunoglobulin heavy chain coding sequences into plant cells and plants produced by such methods .

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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***Remarks***

No claim is allowed.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins  
Primary Examiner  
Art Unit 1638

CC

  
12/19/05